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Attorney Docket No. P31853C1

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	Buckingham, *et al.*	August 24, 2001
Serial No.:	Not Assigned	Group Art Unit No.: Not Assigned
Filed:	Herewith	Examiner: Not Assigned
For:	TREATMENT OF DIABETES WITH THIAZOLIDINEDIONE, INSULIN SECRETAGOGUE AND DIGUANIDE	

PRELIMINARY AMENDMENT

Preliminary to the examination of this application, Applicants respectfully request amendment of the above-identified application as follows:

In the Specification:

Kindly add the Abstract enclosed herewith on a separate sheet, at the end.

In the Claims:

Please amend claims 4-12, 16, 18-20 and 22 as follows:

4. (Amended) A method according to claim 1, wherein the insulin sensitiser is 5-[4-[2-(N-methyl-N-(2-pyridyl)amino)ethoxy]benzyl]thiazolidine-2,4-dione (Compound I).

5. (Amended) A method according to claim 4, which comprises the administration of 2 to 12 mg of Compound (I).

6. (Amended) A method according to claim 5, which comprises the administration of 2 to 4, 4 to 8 or 8 to 12 mg of Compound (I).

7. (Amended) A method according to claim 6, which comprises the administration of 2 to 4mg of Compound (I).

8. (Amended) A method according to claim 6, which comprises the method the administration of 4 to 8mg of Compound (I).

9. (Amended) A method according to claim 6, which comprises the administration of 8 to 12 mg of Compound (I).

10. (Amended) A method according to claim 7, which comprises the administration of 2 mg of Compound (I).

11. (Amended) A method according to claim 8, which comprises the administration of 4 mg of Compound (I).

12. (Amended) A method according to claim 8, which comprises the administration of 8 mg of Compound (I).

16. (Amended) A composition according to claim 14, wherein the insulin secretagogue is glibenclamide, glipizide, gliclazide, glimepiride, tolazamide or tolbutamide, acetohexamide, carbutamide, chlorpropamide, glibornuride, gliquidone, glisentide, glisolamide, glisoxepide, glyclopyamide, glycylamide or repaglinide.

18. (Amended) A composition according to claim 14, wherein the insulin sensitiser is 5-[4-[2-(N-methyl-N-(2-pyridyl)amino)ethoxy]benzyl]-thiazolidine-2,4-dione (Compound I).

19. (Amended) A composition according to claim 14, which comprises 2 to 12 mg of Compound (I).

20. (Amended) A pharmaceutical composition comprising an insulin sensitiser, an insulin secretagogue and a pharmaceutically acceptable carrier therefor, for use as an active therapeutic substance.

22. (Amended) A composition according to claim 14, wherein the insulin sensitiser is (+) -5-[[4-[(3,4-dihydro-6-hydroxy-2, 5, 7, 8-tetramethyl-2H-1-benzopyran-2-yl)methoxy]phenyl]methyl]-2,4-thiazolidinedione (or troglitazone), 5-[4-[(1-methylcyclohexyl)methoxy]benzyl] thiazolidine-2,4-dione (or ciglitazone), 5-[4-[2-(5-ethylpyridin-2-yl)ethoxy]benzyl] thiazolidine-2,4-dione (or pioglitazone) or 5-[(2-benzyl-2,3-dihydro-benzopyran)-5-ylmethyl)thiazolidine-2,4-dione (or englitazone); or a pharmaceutically acceptable form thereof.

REMARKS

Attached hereto is a marked-up version of the changes made to the claims by the current amendment. The attached page is captioned "**Version with markings to show changes made.**"

Applicants have amended the claims to put them in conformity with the U.S. practice.

No new matter has been introduced.

Respectfully submitted,

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the specification:

An Abstract of the Invention has been added.

In the claims:

Claims 4-12, 16, 18-20 and 22 have been amended as follows:

4. (Amended) A method according to [any one of] claim[s] 1 [to 3], wherein the insulin sensitiser is 5-[4-[2-(N-methyl-N-(2-pyridyl)amino)ethoxy]benzyl]thiazolidine-2,4-dione (Compound I).

5. (Amended) A method according to [any one of] claim[s 1 to] 4, which comprises the administration of 2 to 12 mg of Compound (I).

6. (Amended) A method according to [any one of] claim[s 1 to] 5, which comprises the administration of 2 to 4, 4 to 8 or 8 to 12 mg of Compound (I).

7. (Amended) A method according to [any one of] claim[s 1 to] 6, which comprises the administration of 2 to 4mg of Compound (I).

8. (Amended) A method according to [any one of] claim[s 1 to] 6, which comprises the method the administration of 4 to 8mg of Compound (I).

9. (Amended) A method according to [any one of] claim[s 1 to] 6, which comprises the administration of 8 to 12 mg of Compound (I).

10. (Amended) A method according to [any one of] claim[s 1 to 6] **7**, which comprises the administration of 2 mg of Compound (I).

11. (Amended) A method according to [any one of] claim[s 1 to 6] **8**, which comprises the administration of 4 mg of Compound (I).

12. (Amended) A method according to [any one of] claim[s 1 to 6] **8**, which comprises the administration of 8 mg of Compound (I).

16. (Amended) A composition according to claim 14 [or claim 15], wherein the insulin secretagogue is glibenclamide, glipizide, gliclazide, glimepiride,

tolazamide or tolbutamide, acetohexamide, carbutamide, chlorpropamide, glibornuride, gliquidone, glisentide, glisolamide, glisoxepide, glyclopyamide, glycylamide or repaglinide.

18. (Amended) A composition according to [any one of] claim[s] 14 [to 17], wherein the insulin sensitiser is 5-[4-[2-(N-methyl-N-(2-pyridyl)amino)-ethoxy]benzyl]thiazolidine-2,4-dione (Compound I).

19. (Amended) A composition according to [any one of] claim[s] 14 [to 17], which comprises 2 to 12 mg of Compound (I).

20. (Amended) A pharmaceutical composition comprising an insulin sensitiser, an insulin secretagogue and a pharmaceutically acceptable carrier therefor, for use as an active therapeutic substance.

22. (Amended) A composition according to [any one of] claim[s] 14, [20 or 21,] wherein the insulin sensitiser is (+) -5-[[4-[(3,4-dihydro-6-hydroxy-2, 5, 7, 8-tetramethyl-2H-1-benzopyran-2-yl)methoxy]phenyl]methyl]-2,4-thiazolidinedione (or troglitazone), 5-[4-[(1-methylcyclohexyl)methoxy]-benzyl] thiazolidine-2,4-dione (or ciglitazone), 5-[4-[2-(5-ethylpyridin-2-yl)ethoxy]benzyl] thiazolidine-2,4-dione (or pioglitazone) or 5-[(2-benzyl-2,3-dihydrobenzopyran)-5-ylmethyl)thiazolidine-2,4-dione (or englitazone); or a pharmaceutically acceptable form thereof.

ABSTRACT OF THE DISCLOSURE

A method for the treatment of diabetes mellitus and conditions associated with diabetes mellitus in a mammal, which method comprises administering an effective non-toxic and pharmaceutically acceptable amount of an insulin sensitiser, an insulin secretagogue and a biguanide antihyperglycaemic agent, to a mammal in need thereof; and composition for use in such method.